UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,452	11/27/2001	Nissim Benvenisty	BENVENISTY5	2188

1444 7590 06/27/2006

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
TON, THAIAN N	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,452	BENVENISTY ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for raply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failura to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduca any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-17,36 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-17,36 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/30/06 has been entered.

Applicants' Amendment and Response, filed 1/5/06, has been considered and entered. Claims 1, 3, 11-17 and 36 have been amended. Claims 18-35 and 37-56 have been cancelled. Claim 59 has been added. Claims 1-9, 11-17, 36 and 59 are pending and under current examination.

The Benvenisty Declaration under 37 CFR §1.132, filed 4/7/06, has been considered and the Examiner's Response is found in the body of this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11-17, and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The amendment to the claims introduces new matter into the disclosure with regard to the recitation that the method of altering gene expression requires a transfection efficiency greater than obtainable by means of electroporation. Applicants have not pointed specifically to where support for the amendment to the claims can be found. Page 12, lines 7-18 and Example 1, Figure 1 discuss various transfection efficiencies. Although the specification provides guidance with regard to ExGen 500 (cationic polymer) providing greater relative transfection efficiency than electroporation alone (see Figure 1), Fugene (non-liposomal formulation) and Lipofectamine (cationic lipid), both have lower levels of transfection efficiencies than electoporation. The claims, as instantly amended, are not contemplated nor supported by the presently filed disclosure, because there is no support for transfection efficiency greater than that obtainable by electroporation, using the breadth of transfection reagents, as broadly claimed. Thus, the amendment to the claims is determined to introduce new matter into the presently-filed disclosure.

MPEP § 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP § 2163.02 teaches that, "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP § 2163.06 further notes, "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure."

Written Description

Claims 1-3, 7-9, 11-13, 16, 17, and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that, "[A]pplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar,* 19USPQ2d at 1117. The specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

While the specification provides adequate guidance with regard to transfection of hES cells, in the presence of a cationic non-lipid polymer reagent, with a polynucleotide operably linked to a promoter, wherein the polynucleotide encodes a fluorescent protein or an antibiotic resistance protein, the specification fails to describe any other species, within the genus of gene expression altering sequences that show measurably different gene expression after introduction of the polynucleotide, while retaining the pluripotent character of the cells, as instantly claimed and encompassed by the claims, with particularity, to indicate that Applicants had possession of the claimed invention. The specification teaches that a gene expression altering sequence can be an enhancer, or proteins not normally expressed in hES cells, or fluorescent or antibiotic resistance protein (see page 3, lines 1-10). The specification further teaches that an expression altering sequence can be any exogenous nucleic acid that can modulate gene expression, such as enhancers, promoters, or transcription activators. See page 10, lines 1-11. However,

these are general terms, which fail to provide particular guidance as to which exogenous nucleic acids, enhancers, promoters or transcription activators would be used as claimed, and produce the required effects, namely that the gene expression is measurably different before and after transfection, and that the hES cells maintain their pluripotent character. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described by the specification, and which are not conventional in the art **as of Applicants effective filing date**. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient, relevant, identifying characteristics (as it relates to the invention as a whole), such that one skilled in the art would recognize that the inventor had possession of the claimed invention. In the instant case, the claimed embodiments of gene expression altering sequences that show measurably different gene expression after introduction of the polynucleotide, while retaining the pluripotent character of the cells, lack a written description. The specification fails to describe what gene expression altering sequences fall into this genus, when constructed and used as claimed. The skilled artisan could not envision the detailed chemical structure of all of the gene expression altering sequences that would have the properties as claimed, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity. Adequate written description requires more than a mere statement that it is part of the invention.

See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification only provided the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description of 35 U.S.C. 112 is severable from its enablement provision [see p. 1115].

Enablement

Claims 1-9, 11-17, and 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for transfecting human ES cells, comprising introducing a polynucleotide that does not contain viral genes, into a population of human ES cells by transfection in the presence of a cationic non-lipid polymer reagent, wherein said polynucleotide is operably linked to a promoter that encodes a fluorescent protein, or an antibiotic resistance protein;

the specification does not reasonably provide enablement for the breadth of the claims, which include transfection of hES cells in the presence of at least one transfection reagent selected from cationic non-lipid polymer reagent, a non-liposomal reagent, and a cationic lipid agent, wherein the polynucleotide introduced into the hES cell is operably linked to a promoter and contains any gene expression altering sequence, such that the gene expression in the ES cells, prior to introducing the polynucleotide is measurably different from gene expression after introducing the polynucleotide, while retaining the pluripotent character to the cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The claims are drawn to methods of altering gene expression in a population of hES cells, with a transfection efficiency greater than that obtainable by means of electroporation comprising, introduction of a polynucleotide by transfection in the presence of at least one transfection reagent selected from the group consisting of a cationic non-lipid polymer reagent, a non-liposomal reagent, and a cationic lipid agent, wherein the polynucleotide is operably linked to a promoter and contains a gene expression altering sequence such that gene expression in the ES cells, prior to introduction of the polynucleotide, is measurably different from gene expression, after introducing the polynucleotide, while retaining the pluripotent character of the cells, wherein the transfection efficiency is greater than that obtainable by electroporation, and wherein the nucleic acid introduced into the human ES cells does not contain viral genes. Specific embodiments limit the gene expression altering sequence to fluorescent proteins or antibiotic proteins.

The breadth of the claims encompass using any of the transfection reagents (cationic non-lipid, non-liposomal, or cationic lipid). The claims encompass introduction of any gene expression altering sequence into the hES cells, so that introduction of the polynucleotide is measurably different from gene expression before and after introduction of the polynucleotide.

The specification teaches the transfection of hES cells with a Rex-1-EGFP expression vector, and a contruct encoding the firefly Rennila protein under control of the TK promoter, using either electroporation, Lipofectamine™, FuGene™ or ExGen™. See Example 1. Figure 1 clearly shows that the most efficient method for transfection is when ExGen™ is used (see also, p. 19, lines 12-13), and that the other reagents provided efficiencies within the range of electroporation, not greater than. The specification teaches that a gene expression altering sequence can be an enhancer, or proteins not normally expressed in hES cells, or fluorescent or antibiotic resistance protein (see page 3, lines 1-10). The specification further teaches that an expression altering sequence can be any exogenous nucleic acid that

can modulate gene expression, such as enhancers, promoters, or transcription activators. See page 10, lines 1-11.

Applicants disclosure, as well as the various Declarations provided by Applicants show that the state of the art of transfection is such that although one of skill in the art would be aware of the various transfection reagents, as claimed, it was unexpected that using a particular reagent, ExGen™ (a cationic non-lipid polymer reagent) would produce a result of a transfection efficiency greater than all other reagents, including electroporation. See also, #6 of the Benvenisty Declaration filed 4/7/06. Furthermore, the working example in the specification only supports that ExGen is the only reagent that would produce a transfection efficiency that is greater than electroporation.

Furthermore, with regard to the particular gene expression altering sequence that would be introduced into the hES cells, the specification has only taught using fluorescent marker genes or antibiotic resistance genes, in order to practice the claimed method. Although the specification contemplates various sequences that could be used, the specification does not enable these sequences because there is no specific guidance or teaching with regard to particular enhancers or promoters, transcription activators that would both have a measurably different gene expression before and after transfection, and retain the pluripotent character of the hES cells.

With regard to claim 17, which is directed to the knockout of a particular gene, the Examiner notes that Zwaka *et al.*, provided by Applicants, states that, "Although clones were obtained using both transfection reagents, ExGen and FuGene, ... none were the result of homologous recombination. These results are consistent with the observation that transfection using lipid and cationic reagents results in inefficient homologous recombination in other mammalian cell types, and that physical methods of introducing DNA are, in general, more effective." See page 319, col. 1-2, bridging sentence. Thus, given that claim 17 is directed to a method of

specifically knocking out a gene, by gene targeting, using a cationic polymer, and that post-filing art supports the unpredictability in successful gene targeting to knockout a specific gene of interest in hES cells using these same reagents, one of skill in the art would have had to practice undue experimentation, at the time of filing, to knockout a particular gene of interest, using a cationic polymer, as required by claim 17.

Accordingly, in view of the unpredictable state of the art of transfection of hES cells, and Applicants' working examples, Declarations and arguments, it would have required undue experimentation, for one of skill in the art, to use any of the reagents, other than cationic non-lipid polymers, to transfect hES cells, with a gene expression sequence, whose expression is measurably different before and after transfection, while retaining the pluripotent character of the hES cells, as instantly claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11-17, and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "with a transfection efficiency greater than that obtainable by means of electroporation" in claims 1 and 11 is a relative term which renders the claim indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term is indefinite because the transfection efficiency of any given experiment is relative. Claims 2-9 and 59 depend from claim 1; claims 12-17 depend from claim 11.

Claim 1 recites the limitation "the nucleic acid" in the second to last line of the claim. There is insufficient antecedent basis for this limitation in the claim. Claims 2-9 and 59 depend from claim 1.

Claim 11 recites the limitation "the nucleic acid" in the second to last line of the claim. There is insufficient antecedent basis for this limitation in the claim. Claims 12-17 depend from claim 11.

Response to Declaration and Applicants' Arguments

Benevenisty Declaration & Arguments. The Benvenisty Declaration, filed 4/7/06, has been considered, but is not found to be persuasive. The Declaration is provided to clarify the record, concerning the generation of a substantially pure stably transfected population of pluripotent human ES cells, wherein the cells are modified to contain a gene expression altering sequence of DNA. Applicants argue that although Smith teach methods for isolating, and/or enriching and/or selectively propagating animal stem cells, because mouse ES cells are different than human ES cells, the methodology of transfection in murine cells is distinct from that in human cells. Particularly, the Declaration states that electroporation in mouse ES cells is inefficient in human ES cells, and that alternative methodology had to be established in order to arrive at the substantially pure population of stably transfected cells, and further, because human ES cells do not grow well in dilution, it would have been impossible to arrive at stably transfected cells, using an inefficient transfection method, such as electroporation (see page 2 of the Declaration). Further, Applicants argue that if the Examiner's assumption were accurate, there would have been no difficult, for other researchers in the field to have succeed in generating a substantially pure stably transfected population of pluripotent human ES cells. Particularly, the Declaration states that two hindering technical issues should be considered when referring to the generation of stably transfected population of human ES cells, firstly, that transfection protocols that

worked successfully for murine systems were not applicable to human ES cells, and that when human ES cells are too diluted in culture they tend to die. The Declaration states that the particular methodology developed in their laboratory enabled the successful transfection of hES cells, with exogenous DNA, using a chemical reagent, particularly a cationic non-lipid polymer reagent. The Declaration further argues that the Examiner's prior rejection, which is based upon the knowledge available to one at the time of filing, could have electroporated hES cells, to provide a single viable clone, and would not interfere with the final result, is not what actually occurs in when practiced. The Declaration points to the concept of dilution with regard to hES cells, and particularly, that there is a feedback mechanism between human ES cells, and murine feeder cells, such that if the human stem cells are too diluted in culture, they will not survive. Thus, the Declaration states that even if a single clone is obtained, it is likely that it would not survive (see pages 4-5 of the Declaration and pages 12-13 of Applicants' Response). Furthermore, the Declaration states that in order to reach stable transfection, less diluted conditions are needed. Thus, to achieve stable transfection, a good transfection yield is required such there are a sufficient number of cells to initiate the cloning process. This argument is similarly stated in Applicants' response, page 14. Applicants provide Amit *et al.* for support for the concept of dilution when culturing hES cells.

The Declaration and Applicants' arguments refer to Zwaka *et al.*, which discusses homologous recombination in hES cells, following their transfection, and state that electroporation yields substantially lower rates. Finally, the Declaration states that one would not start cloning with very low cell numbers, because one would not expect this small number of cells to produce a substantially pure, stably transfected line. Thus, the Declaration states that for the generation of substantially pure stably transfected population of pluripotent hES cells, the

laboratory overcame the technological obstacles of transfecting hES cells, and isolating a clonal population. See pages 5-6 of the Declaration.

Response to Declaration. Applicants' appear to be arguing unexpected results with regard to their invention, particularly, that only using a cationic, non-lipid polymer reagent (ExGen500), were Applicants able to achieve transfection efficiency greater than that obtainable by electroporation and overcome the technological obstacles of transfecting hES cells. See Figure 1, Example 1, and #6 of the Benvenisty Declaration filed 4/7/06. Thus, the Examiner withdraws the rejections of the claims over §103 in view of these unexpected results. However, a new rejection, with regard to a scope enablement, with regard to the utilizing a cationic, non-lipid polymer reagent to be used in transfection, appears below.

With regard to claim 36, which is directed to a substantially pure, stably transfected population of hES cells, the Declaration, Applicants' arguments Amit *et al.* have been fully considered, but are not persuasive. Claim 36 does not require a particular yield of cells, it only requires a substantially pure population of stably transfected hES cells. The Declaration and Applicants' arguments point to Table 1, of Amit *et al.*, to support low cloning efficiency of hES cells. However, Amit *et al.* teach that using serum replacer produced a several fold increase in cloning efficiency, and that even with this low cloning efficiency (0.83%), they were able to produce clonal hES cell lines. See page 272-273, bridging ¶. Thus, even if a low percentage of hES cells were transfected by electroporation, it would still be possible to produce a stably transfected, clonal population of these cells.

Zwaka *et al.* has been fully considered, but not persuasive. Although the Examiner agrees, given the working examples and Declarations provided, that electroporation may not be an extremely efficient method of transfecting a population of hES cells, because even one cell, could be used to produce a clonal hES cell line, as evidenced by Amit *et al.* The claims require no specific efficiency or

yield to constitute a population of stably transfected hES cells. Thus, the prior art rejection over claim 36 is maintained.

Applicants' Arguments. Applicants argue that Smith has absolutely no examples with regard to hES cells, and indeed all of the examples use murine ES cells, which are much easier to deal with than hES cells. Further, because Smith lists a number of means of introducing selectable markers into cells, the only method used in their examples is electroporation. Applicants argue that in order to anticipate, a reference must show every feature of the claims, and that the Examiner is apparently taking the position that one, following the procedures of Smith, would inherently obtain substantially pure, stably transformed hES cell lines. Applicants argue that here, the fact that a substantially pure, stably transfected population of pluripotent human ES cells could possibly occur, if human cells are selected from the varying kinds of animal cells disclosed in smith, and if a proper selection of introduction means is used, from the myriad of such means, described by Smith, does not establish that the claimed subject matter of claim 36 is inherently disclosed by Smith. Applicants argue that the mouse tests using electroporation certainly do not establish that obtaining a substantially pure, stably transfected population of pluripotent hES cells necessarily occurs, following the procedures of Smith, particularly in view of scientific explanations provided, and the Amit *et al.* publication. See pages 14-16 of the Response.

Response to Arguments. These arguments are considered, but not persuasive. Indeed, Smith provides various means with which one would transfect cells. The claims are drawn to cells, not methods of producing the cells. The methods taught by Smith could all be employed to transfect hES cells, and given Applicants' arguments, Declarations and cited art of record, one could use various means to transfect hES cells, including electroporation, as well as other embodiments, contemplated by Smith. Amit *et al.*, as stated above, show that although efficiency is not high, when using a single cell, one could establish a clonal

hES cell line. The prior rejection of claim 36, by Smith, under §102 (b) is proper and maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The prior rejection of claim 36 under 35 U.S.C. 102(a) or 35 U.S.C. 102(e) as being anticipated by Smith *et al.* is *maintained* for reasons of record advanced in the prior Office action, mailed 11/17/04. The Examiner has addressed each point with regard to Applicants' arguments and Declaration above.

Smith anticipates the claimed invention because they teach methods of transfection of any mammalian embryonic stem cell, which include human ES cells. The method of producing these transfected cells does not depend on its method of production. Accordingly, it is maintained that Smith anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The rejections of the claims 1-4, 6, 7, 11-16, 36, 59 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.*, in view of Fasbender *et al.*, is withdrawn.

The prior rejection of claims 5 and 14 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.* when taken with Fasbender and Myers is withdrawn.

The prior rejection of 17 under 35 U.S.C. 103(a) as being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.* in view of Fasbender *et al.* and further in view of Pascolo *et al.* is withdrawn.

The prior rejection of claims 8 and 9 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.* in view of Fasbender *et al.* and further in view of the Gibco BRL catalog is withdrawn.

The above rejections are withdrawn in view of Applicants' arguments and Declaration, with regard to the unexpected result, namely that utilizing a cationic, non-lipid polymer reagent, Applicants found transfection efficiency greater than that obtainable by means of electroporation.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tnt
Thaian N. Ton
Patent Examiner
Group 1632

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER